space of the renal artery to precisely deliver micro-volumes of alcohol to directly target the nerves. Alcohol is administered using a single infusion in the main renal artery. Doses of 0.15 to 0.6 mL have been studied in this model. The denervation produced with alcohol has been characterized with histology, immunostaining and measurement of renal norepinephrine (NE) in a porcine model. A direct comparison of the denervation produced with alcohol vs. RF was performed using the same model and methods (3 mos. survival). For the RF group 4 renal artery ablations were performed, with one ablation per quadrant.

RESULTS Renal denervation with alcohol creates consistent, dose-related and substantial sympathetic nerve injury. The Peregrine catheter delivers the alcohol directly within the adventitia and peri-adventitial space. Because the alcohol is infused outside of the vessel wall, changes to the media are rare; typically mild and focal; and at the abluminal surface of the media. This contrasts with RF, which typically creates focal transmural medial injury. The ablation area produced by the infusion of alcohol is larger, and typically circumferential, in comparison to the focal ablation produced by RF. Ablation depth (distance from the lumen) and area (morphometric) were significantly greater for alcohol using 0.3 mL and 0.6 mL per artery, compared to RF. Depth ($p<0.05$ for both alcohol doses) compared to RF: 0.3 mL = 6.6±1.2 mm, 0.6 mL = 8.2±2.2 mm, RF = 3.9±1.2 mm. Area ($p=0.0001$): 0.3 mL = 30.8±13.7 mm2, 0.6 mL = 41.6±7.5 mm2, RF = 11.0±7.5 mm2. Compared to controls the median NE was reduced by 83% for 0.6 mL, 76% for 0.3 mL and 66% for RF ($p=0.095$ both alcohol vs. RF). The median procedure time for the alcohol groups was 9 min. vs. 29 min. for RF ($p<0.05$). Neither RF nor alcohol infusion produced any systemic or renal adverse events.

CONCLUSIONS The use of alcohol with the Peregrine System for "chemical" renal denervation appears to be potentially safer and more time efficient than RF. Alcohol-mediated denervation appears to address the issue of adequacy of denervation by demonstrating superior coverage in terms of ablation depth and area, yielding a greater reduction in renal NE vs. RF. Chemical denervation can also be performed in very short renal arteries, avoiding technical issues and adverse events associated with treating the entire length of the artery, or the distal branches as has been proposed for RF. Overall, chemical denervation using alcohol may represent a promising alternative to RF ablation.

CATEGORIES ENDOVASCULAR: Hypertension Therapies and Renal Denervation

KEYWORDS Hypertension, Peripheral, Renal denervation

TCT-89

Renal Sympathetic Denervation in Treatment Resistant Essential Hypertension. A Sham-Controlled, Double-blinded Randomized Trial (ReSET trial)

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BACKGROUND Renal denervation (RDN) for the treatment of resistant hypertension has been shown in pilot studies to lower blood pressure (BP) without safety alerts. However, this was only shown in open la-belled study designs and has primarily addressed the effect on office BP. We therefore conducted a sham controlled, double blind randomized single center trial to establish reliable efficacy data based on 24-h BP measurements. We expected a 10 mmHg reduction in ABPM systolic daytime BP (ASBP-day) at 3 months in the RDN group as compared to SHAM, and planned to randomize 70 patients.

METHODS Patients with therapy resistant essential hypertension, 30 to 70 years of age, were randomly as-signed to undergo RDN or a sham procedure. Inclusion criteria were ASBP-day $\geq$ 145 mmHg follow one month of stable medication and 2 weeks of compliance registration. Recruitment and patient follow-up was held in seven dedicated hypertension out-patient clinics. Drug treatment was optional, apart from the mandatory use of a diuretic when tolerated by the patient. Follow-up changes in antihypertensive medication were only allowed if requested by the patient or if harm-full changes in BP or safety parameters occurred. Renal artery anatomy was evaluated by CT angio in advance. All RDN procedures were carried out by the same experienced operator using the simplicity catheter (Medtronic).

RESULTS 69 patients, mean age 56 ± 9 year, were randomized for RDN (n = 36) or SHAM (n = 33). One patient suffered a NSTEMI close to randomization and was excluded. Groups showed similar demography and baseline parameters. Mean baseline ASBP was 159 ± 12 mmHg (RDN) and 159 ± 14 mmHg (SHAM). Groups had similar reductions in ASBP compared to baseline at 3 months: - 6.2 ± 18.8 mmHg (RDN) vs. - 6.0 ± 13.5 mmHg (SHAM) and at 6 months: - 6.1 ± 18.9 mmHg (RDN) vs. - 4.3 ± 15.1 mmHg (SHAM). Mean antihypertensive DDD usage at 3 month was equal 6.8 ± 2.7 (RDN) vs. 7.0 ± 2.5 (SHAM), although more RDN patients (41 %) had medical changes than SHAM pt (24 %).

CONCLUSIONS Renal denervation performed at a single center and by a high volume operator reduced ASBP to the same level as SHAM treatment. This result is in line with findings from the HTN3 trial.

CATEGORIES ENDOVASCULAR: Hypertension Therapies and Renal Denervation

KEYWORDS Clinical Trial, Hypertension, Renal sympathetic denervation

TCT-90

Sustained Beneficial Effects of Multi-Electrode Renal Denervation on Cardiac Adaptations In Resistant Hypertension: A 24-Months Follow-Up Study

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BACKGROUND In this study we investigated whether multi-electrode catheter-based renal sympathetic denervation (RDN) has favorable effects on left ventricular (LV) structural and functional indices in patients with resistant hypertension after a follow-up of 24 months.

METHODS Twenty patients with resistant hypertension [age: 57±10 years, 13 males, office blood pressure (BP): 182/97±19/18 mmHg under 4.5±0.6 drugs] who underwent RDN were followed-up for 24 months. A full transthoracic echocardiographic study was performed in all patients and LV mass was calculated using the Devereux formula and was indexed for body surface area and height.

RESULTS Average office BP was reduced to 148±21/85±14 mmHg at 12 months and to 143±23/80±14 mmHg at 24 months ($p<0.001$ for all). In the RDN group, LV mass index was significantly reduced from 136±20.1 g/m2 (56.5±8.7 g/m2.7) to 121±16.6 g/m2 (50.6±6 g/m2.7) at 12 months and to 115.6±23.3 g/m2 (48.8±9.3 g/m2.7) at 24 months ($p<0.01$ for all+). RDN decreased mean interventricular septum thickness from 12.1±1.2 mm to 11.4±0.9 mm at 12 months and to 11.3±0.9 mm at 24 months ($p<0.05$ for all). After RDN, the number of patients with concentric LV hypertrophy (i.e. relative wall thickness>0.42 and LV mass>48 g/m2.7 for male and >44 g/m2.7 for female) decreased from 16 patients (80%) at baseline to 10 patients (50%) at 12 months, and to 7 patients (36.8%) at 24 months. Regarding diastolic function RDN caused an increase in mitral valve E′/A′ ratio from 0.62±0.28 to 0.70±0.25 at 12 months and to 0.84±0.32 at 24 months ($p<0.05$ for all) and a decrease in the E/E′ ratio from 14.8±6.1 to 11.8±3.7 at 12 months and to 9.7±4 ($p<0.05$ for all).

CONCLUSIONS This the first study to show that multi-electrode RDN system results in a significant and sustained improvement of diastolic function and attenuation of LV mass index in increased cardiovascular risk resistant hypertensive patients after a follow-up of 24 months. These results suggest pleiotropic cardiovascular benefits of RDN therapy in the setting of resistant hypertension.

CATEGORIES ENDOVASCULAR: Hypertension Therapies and Renal Denervation